Kidney and Gastrointestinal Diseases

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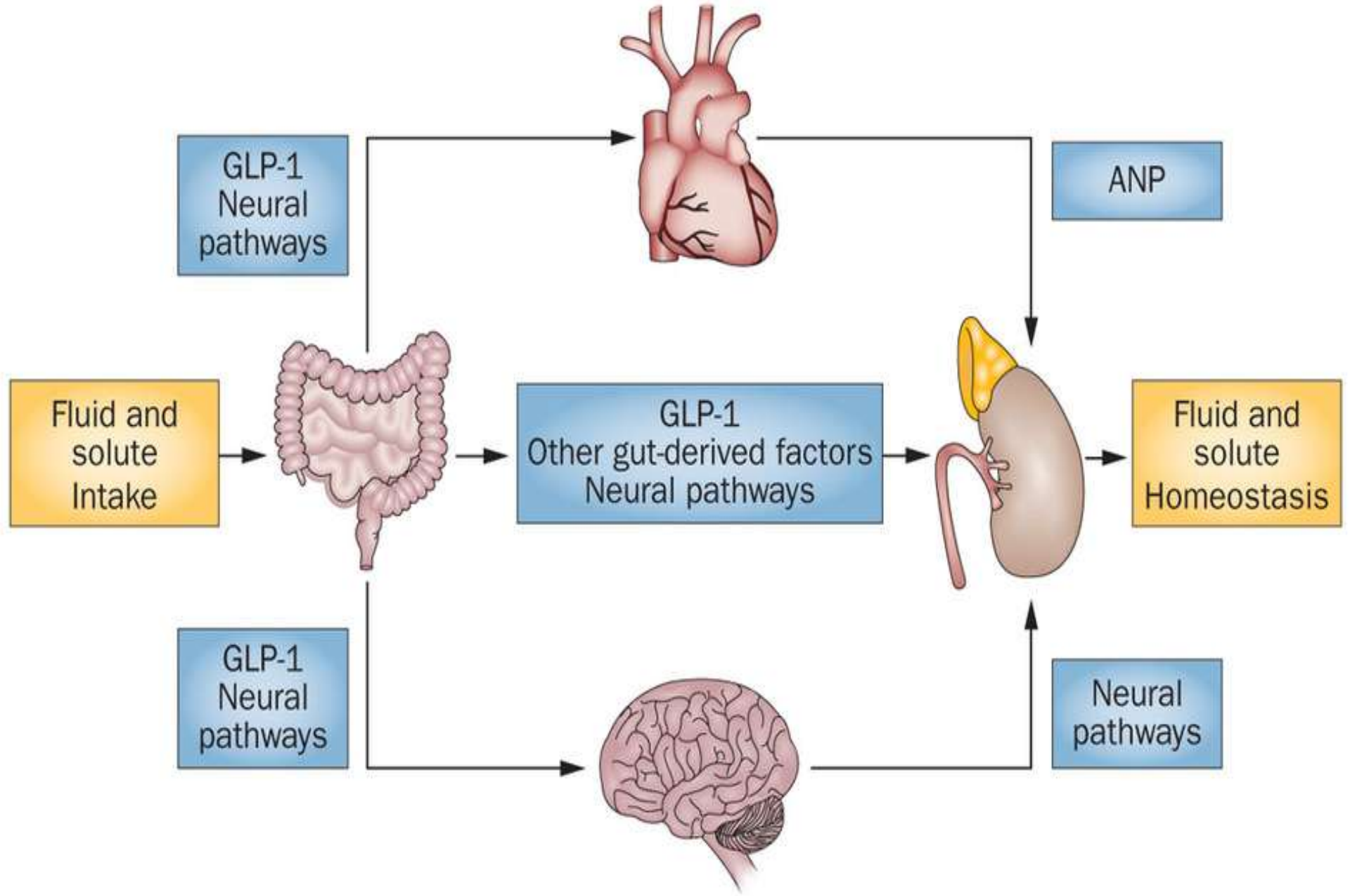
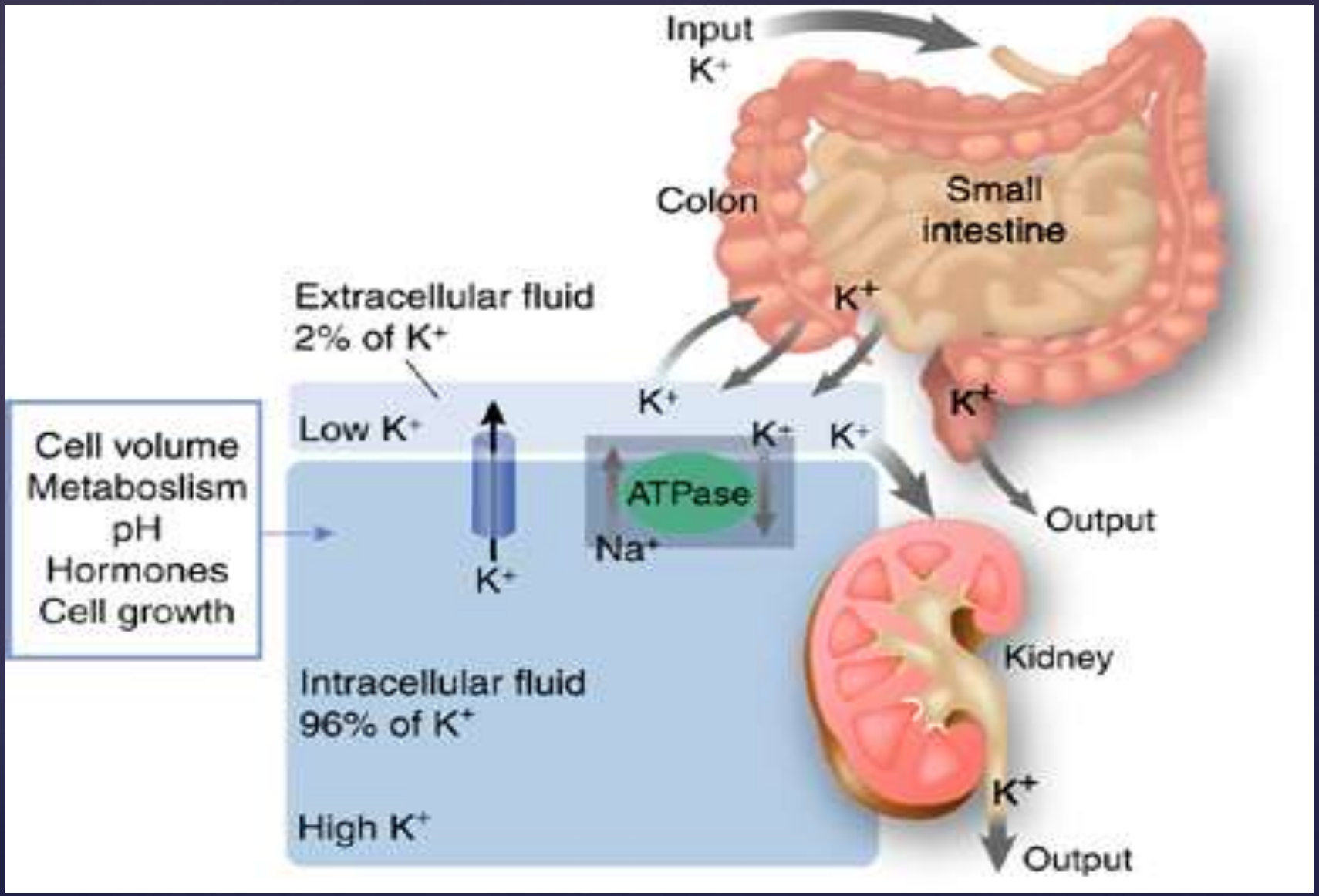
Potential regulatory links between the gastrointestinal tract and the kidney involve neurohormonal interactions.

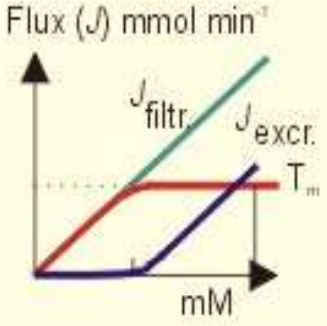
Several gut-derived factors (including GLP-1, guanylin, uroguanylin, secretin, vasoactive intestinal peptide, ghrelin, gastrin and cholecystokinin) and neural signals related to dietary intake and composition are thought to affect renal functi


GLP-1
Neural
pathways
ANP
Fluid and
solute
Intake
GLP-1
Other gut-derived factors
Neural pathways
Fluid and
solute
Homeostasis
GLP-1
Neural
pathways
Neural
pathways


Input
K+
Colon
Small intestine
Extracellular fluid
2% of K+
K+
K+
K+
K+
K+
Low K+
ATPase
Na+
K+
Output
Cell volume
Metaboslism
pH
Hormones
Cell growth
Kidney
Intracellular fluid
96% of K+
High K+
K+
Output

Daily Calcium Balance

all numbers without units are mg per day [mmol daily]



1000 [25]

PTH

Nephron

Filtration flux:
10 000 [250]

Stomach

Secretion: 150

+
9800

+

Absorption: 400 [10]

Total plasma-[Ca]: 2.5 mM

Plasma-[Ca^{2+}]: 45% free ions

500

50

Bone

Excretion flux:
200 [5]

Faecal excretion: 750 [19]

Fig. 30-3

KMc

RENAL INVOLVEMENT IN ACUTE GASTROENTERITIS;

Acute gastroenteritis is a common problem in developing countries.

The most common complication of acute diarrhea is dehydration leading to hypovolemia and further complications like acute kidney injury.

Acute gastroenteritis leads to hypovolemia and then may cause acute kidney injury. Acute renal failure secondary to acute gastroenteritis is still a common problem

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Early referral to the tertiary care hospital and timely management with parenteral or/and oral rehydration solution can reduce risk of development of acute renal failure in patients with acute gastroenteritis.

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The kidneys in inflammatory bowel disease

Extraintestinal manifestations and complications are common in patients with inflammatory bowel disease (IBD) and can involve almost any organ or system.

Renal or urinary complications occur in 4-23% of patients, often in those with severe long-standing disease

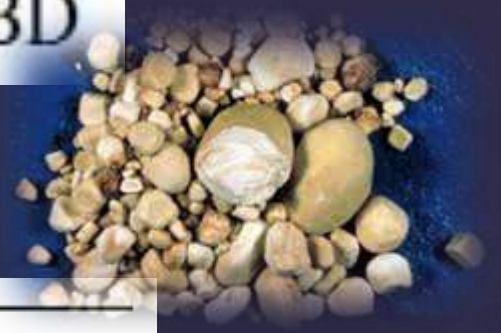
Renal complications in IBD

1. Glomerulonephritis (from minimal change nephropathy to rapidly progressive crescentic GN)
2. Tubulointerstitial abnormalities (interstitial nephritis, granoulomatous interstitial nephritis, nephrocalcinosis, renal tubulor acidosis)
3. Amyloidosis
4. Renal hypertension
5. Iatrogenic complications: medications, aminosalicylates, cyclosporine, xylitol at high dose, sodium phosphate (colon cleansing)
6. Miscellaneous complications
7. Pyonephrosis/Pyelonephritis

Urologic complications in IBD

1. Fistulas
   - enterovesical
   - rectovesical
   - rectourethral
   - anourethral
   - urethrocutaneous
   - vesicocutaneous
   - ileoureteral
   - enterourachovesical
   - ileal pouch-vesical
2. Acute/chronic pyelonephritis
3. Nephrolithiasis (uric acid, calcium oxalate, calcium phosphate)
4. Non calculous obstructive uropathy
5. Genital involvement (penis, scrotum, vulva, prostate gland)
6. Iatrogenic complications (Surgical complications)
7. Miscellaneous complications

Stone types and pathophysiology in IBD



Stone type	Risk factors
1. Uric acid	Diarrhea, ileostomy, hyperurichemia
2. Calcium oxalate	Ileal resection or disease,enteric hyperoxaluria
3. Calcium phosphate	Bed rest, steroids,increased urine Ca (mobilization from bone and de creased ubularresorption of Ca)

Laboratory methods of assessing renal deterioration in IBD

1. Glomerular toxicity:
   - albumin
   - transferrin
2. Proximal tubular damage
   - *membrane-bound enzymes*

   a. Alaninoaminopeptidase (AAP)

   b. Dipeptidylpeptidasse 4 (DDP4)

   c. Aminopeptidase M

   d. Intestinal type alkaline phosphatase

   e. γ-Glutamyl transferase (γ-GT)

   - *lysosomal enzymes*

   a.N-acetyl-beta-D-glucosaminidase (b-NAG)

   - a1-microglobulin
   - b2-microglobulin

3. Clearance of creatinine
4. Urine microscopy.
5. Clinical chemistry (urea, creatinine, K,Na etc)
6. Distal tubulαr damage
   - Tamm-Horsfall protein
   - Glutathione transferase π
7. renal biopsy evaluation
   - light microscopy
   - immunohistochemistry
   - electron microscopy
8. Radiology
   - routine radiology (excrectory urography,pyelography).
   - C.T, MRI
9. Nuclear medicine/scintigraphy

Other Associations with IBD
Renal Involvement

- The rare triad **sclerosing cholangitis**, **IBD** and **gromerulonephritis** has twice been reported.

- Non specific **ulcerative rectocolitis** and **LE** with **renal involvement** has been reported.

- **IBD**, **ankylosing spondylitis**, associated **cutaneous vasculitis**, **glomerulonephritis** and **circulating IgA complexes** have been reported in two patients.

RENAL HYPERTENSION IN IBD

- Renal hypertension usually develops as a complication of renal failure in IBD as result of *amyloidosis* and is clinically expressed as nephrotic syndrome with peripheral edema.

- Renal hypertension can also be the presenting symptom of an asymptomatic non calculus obstructive uropathy or as a result of chronic cyclosporine toxicity (arteriolopathy, interstitial fibrosis and tubular atrophy).

NEPHROTOXIC DRUGS IN IBD

Reported nephrotoxicity of drugs used in IBD

1. Aminosalicylates (5-ASA, mesalamine, sulfasalazine, olsalazine)
   - glomerulonephritis
   - interstitial nephritis
   - minimal change nephropathy with nephrotic syndrome
   - in utero exposure (mesalamine)-Kidney absence and ureter abnormalities in neonate
   - tubulo-interstitial nephritis
2. Cyclosporine
   - arteriolopathy- striped interstitial fibrosis-tubular atrophy
3. Xylitol
   - oxalate stone formation in parenchyma (renal, brain)
   - death
4. Sodium phosphate enemas
   - acute renal failure due to dehydration during colonic cleansing.
5. Non steroid antinflammatory drugs (naproxen)
   - interstitial nephritis

CELIAC DISEASE

Celiac disease (CD) is an autoimmune disorder occurring worldwide with a prevalence of about 1% of the Western population.

The classic presentation comprises symptoms of malabsorption such as diarrhea and weight loss, but the spectrum of symptoms is wide, including asymptomatic disease

End-stage renal disease

- Patients with primary glomerulonephritis often display an activated mucosal immune system, increased gut permeability and an increased number of mucosal intra-epithelial T-lymphocytes.

- Furthermore, CD autoantibodies have been observed in individuals with renal disease.

- Some renal disease will improve on a low-antigenic diet lacking in gluten

- Previous research has suggested an association between CD and renal disease.
- Collin et al showed an increased prevalence of CD among individuals with *IgA nephropathy*.
- Peters et al showed an increased mortality rate of *nephritis* in individuals with CD
- This finding was supported by a study reporting an increased risk of dialysis and renal transplantation in CD.

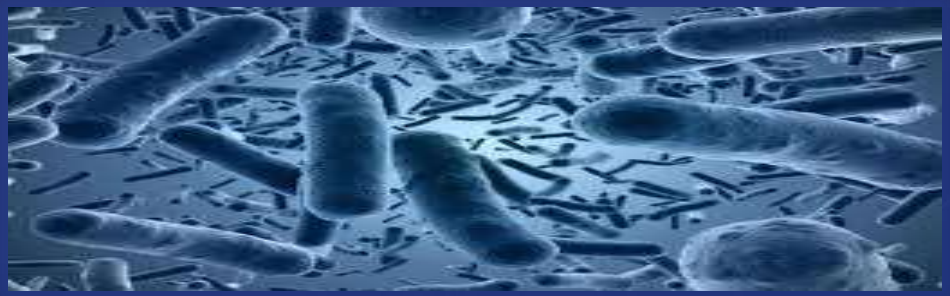
- Reported cases ;two children, one with *nephrotic syndrome* and other with *vesical calculus* that were later confirmed to have an underlying celiac disease.

Clostridium difficile

- Clostridium difficile infection is primarily a nosocomial infection but asymptomatic carriers of Clostridium difficile can be found in up to 5% of the general population.

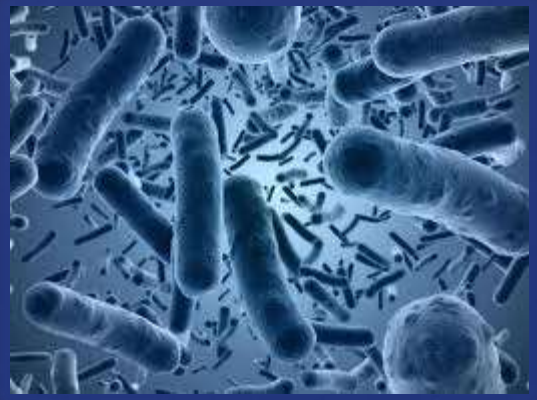
- Ampicillin, cephalosporins and clindamycin are the antibiotics that are most frequently associated with Clostridium difficile-associated diarrhea or colitis.

- Little is known about acute renal failure as a consequence of Clostridium difficile-associated diarrhea.

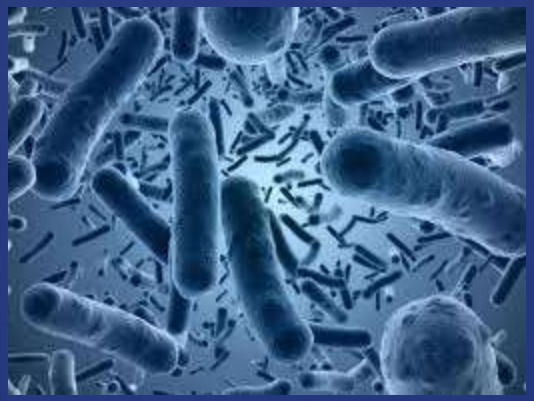


- The link between Clostridium difficile-associated diarrhea and acute renal failure in our patient was most likely volume depletion.

- However, in experimental studies a direct influence of Clostridium difficile toxins on renal duct cells could be shown.



- Rapid diagnosis, nonspecific supportive treatment and specific antibiotic treatment, especially in the elderly, may lower excess mortality Clostridium difficile-associated diarrhea and renal failure being possible complications.




Thank you
wiseGEEK